WO 2005/014550 PCT/EP2004/008972

CLAIMS

1. A compound of formula (I):

5

10

15

20

25

30

(1)

wherein

 $\rm R^{1}$ is selected from hydrogen, C₁₋₆alkyl optionally substituted by up to three groups independently selected from C₁₋₆alkoxy, halogen and hydroxy, C₂₋₆alkenyl, C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, phenyl optionally substituted by up to three groups independently selected from R⁵ and R⁶, and heteroaryl optionally substituted by up to three groups independently selected from R⁵ and R⁶,

 R^2 is selected from hydrogen, C_{1-6} alkyl and - $(CH_2)_q$ - C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups,

or $(CH_2)_mR^1$ and R^2 , together with the nitrogen atom to which they are bound, form a four- to six-membered heterocyclic ring optionally substituted by up to three C_{1-6} alkyl groups;

R³ is chloro or methyl;

 R^4 is the group -NH-CO- R^7 or -CO-NH-(CH₂)_g- R^8 ;

 $\rm R^5$ is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_q-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, -CONR⁹R¹⁰, -NHCOR¹⁰, -SO₂NHR⁹, - (CH₂)₈NHSO₂R¹⁰, halogen, CN, OH, -(CH₂)₈NR¹¹R¹², and trifluoromethyl;

 R^6 is selected from C_{1-6} alkyl, C_{1-6} alkoxy, halogen, trifluoromethyl and - $(CH_2)_sNR^{11}R^{12}$;

 R^7 is selected from hydrogen, C_{1-6} alkyl, - $(CH_2)_q$ - C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups, trifluoromethyl, - $(CH_2)_r$ heteroaryl optionally substituted by R^{13} and/or R^{14} , and - $(CH_2)_r$ phenyl optionally substituted by R^{13} and/or R^{14} ;

 R^8 is selected from hydrogen, C₁₋₆alkyl, C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, CONHR⁹, phenyl optionally substituted by R¹³ and/or R¹⁴, and heteroaryl optionally substituted by R¹³ and/or R¹⁴;

WO 2005/014550 PCT/EP2004/008972

 ${\sf R}^9$ and ${\sf R}^{10}$ are each independently selected from hydrogen and ${\sf C}_{1\text{-}6}$ alkyl,

or R^9 and R^{10} , together with the nitrogen atom to which they are bound, form a five- to six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵, wherein the ring may be substituted by up to two C_{1-6} alkyl groups;

 R^{11} is selected from hydrogen, C_{1-6} alkyl and - $(CH_2)_q$ - C_{3-7} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups,

R¹² is selected from hydrogen and C₁₋₆alkyl,

5

10

15

20

25

30

or R¹¹ and R¹², together with the nitrogen atom to which they are bound, form a five or six-membered heterocyclic ring optionally containing one additional heteroatom selected from oxygen, sulfur and N-R¹⁵;

 R^{13} is selected from C₁₋₆alkyl, C₁₋₆alkoxy, -(CH₂)_q-C₃₋₇cycloalkyl optionally substituted by one or more C₁₋₆alkyl groups, -CONR⁹R¹⁰, -NHCOR¹⁰, halogen, CN, -(CH₂)_sNR¹¹R¹², trifluoromethyl, phenyl optionally substituted by one or more R¹⁴ groups and heteroaryl optionally substituted by one or more R¹⁴ groups;

 R^{14} is selected from C₁₋₆alkyl, C₁₋₆alkoxy, halogen, trifluoromethyl and -NR¹¹R¹²:

R¹⁵ is selected from hydrogen and methyl;

X and Y are each independently selected from hydrogen, methyl and halogen;

m is selected from 0, 1, 2, 3 and 4, wherein each carbon atom of the resulting carbon chain may be optionally substituted with up to two groups selected independently from C_{1-6} alkyl and halogen;

q is selected from 0, 1 and 2;

r is selected from 0 and 1; and

s is selected from 0, 1, 2 and 3;

or a pharmaceutically acceptable derivative thereof.

- 2. A compound according to claim 1 wherein R^1 is selected from C_{1-6} alkyl optionally substituted by up to three groups independently selected from C_{1-6} alkoxy, halogen and hydroxy, and phenyl optionally substituted by up to three groups independently selected from R^5 and R^6 .
- 3. A compound according to claim 1 or claim 2 wherein R² is hydrogen.
- 35 4. A compound according to any one of the preceding claims wherein R³ is methyl.
 - 5. A compound according to any one of the preceding claims wherein X is fluorine.
- 6. A compound according to any one of the preceding claims wherein R^4 is -CO-NH-40 $(CH_2)_q$ - R^8 .
 - 7. A compound according to any one of the preceding claims wherein R^8 is C_{3-6} cycloalkyl optionally substituted by one or more C_{1-6} alkyl groups.

WO 2005/014550 PCT/EP2004/008972

8. A compound according to claim 1 or a pharmaceutically acceptable derivative thereof substantially as hereinbefore defined with reference to any one of Examples 1 to 20.

5

10

20

40

- 9 A compound according to any one of the preceding claims selected from: 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-(2,2-dimethylpropyl)-3-pyridinecarboxamide 1-oxide;
- 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-[(1*R*)-1,2,2-trimethylpropyl]-3-pyridinecarboxamide 1-oxide;
- 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-N-(1,1-dimethylpropyl)-3-pyridinecarboxamide 1-oxide;
 - 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-(1-ethylpropyl)-3-pyridinecarboxamide 1-oxide;
- 15 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-[(1*S*)-1,2,2-trimethylpropyl]-3-pyridinecarboxamide 1-oxide;
 - 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-[(1*R*)-1,2-dimethylpropyl]-3-pyridinecarboxamide 1-oxide;
 - 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-[(1*S*)-1,2-dimethylpropyl]-3-pyridinecarboxamide 1-oxide; and
 - 6-{5-[(cyclopropylamino)carbonyl]-3-fluoro-2-methylphenyl}-*N*-[(3,4-dimethylphenyl)methyl]-3-pyridinecarboxamide 1-oxide; and pharmaceutically acceptable derivatives thereof.
- 25 10. A pharmaceutical composition comprising at least one compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in association with one or more pharmaceutically acceptable excipients, diluents and/or carriers.
- 11. A method for treating a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase comprising administering to a patient in need thereof a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof.
- 12. A compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof for use in therapy.
 - 13. Use of a compound as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof in the manufacture of a medicament for use in the treatment of a condition or disease state mediated by p38 kinase activity or mediated by cytokines produced by the activity of p38 kinase.

14. A process for preparing a compound of formula (I) as claimed in any one of claims 1 to 9 or a pharmaceutically acceptable derivative thereof which comprises reacting compound of formula (II)

5

(II)

in which R^1 , R^2 , R^3 , R^4 , X, Y and m are as defined in claim 1, with an oxidising agent.